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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,294	05/31/2006	Revel Michel	REVEL17	3323
1444	7590	02/15/2011	EXAMINER	
Browdy and Neimark, PLLC 1625 K Street, N.W. Suite 1100 Washington, DC 20006			WANG, CHANG YU	
ART UNIT	PAPER NUMBER			
1649				
MAIL DATE	DELIVERY MODE			
02/15/2011		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,294	Applicant(s) MICHEL ET AL.
	Examiner CHANG-YU WANG	Art Unit 1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 30 November 2010.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1,3,5,7,8 and 54-60 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1, 3, 5, 7, 8 and 54-60 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-448)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____

5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed 11/30/10 is acknowledged. Claims 2, 4, 6, and 9-53 are cancelled. Claim 57 is amended. Claims 1, 3, 5, 7, 8 and 54-60 are pending in this application and under examination in this office action.
2. Applicant's arguments filed on 11/30/10 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

3. The rejection of claim 57 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 11/30/10, the following rejections are maintained.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The rejection is maintained for the reasons made of record and the reasons set forth below.

On p. 7-8 of the response, Applicant argues that claim 54 does not always require other growth factors in culture medium. Applicant argues that the specification teaches that "gp130 activator is added to the NS cells... either alone or together with other growth or differentiation agents....". Applicant argues that the examiner improperly import claim limitations from the specification. Applicant's arguments have been fully considered but they are not persuasive.

In response, contrary to Applicant's arguments, the examiner did not improperly import the claim limitations from the specification. Instead, the claim limitation was properly interpreted in light of the specification because if the basic culture medium recited in the specification does not contain other growth agents, the neurosphere cells can not survive.

In this case, as previously made of record, the basic culture medium for growing neurospheres or generating oligodendrocytes recited in specification has already contained different growth agents (more than one) to maintain and promote cell survival. In particular, the culture medium for NS cells described in the specification contains DMEM/F12, heparin, FGF-2, insulin, transferring, putrescine, selenite, progesterone (p. 14 & p. 29) and the differentiation medium contains DMEM/F12 with insulin, transferrin, putrescine, selenite, progesterone (see p. 29). Although some of these agents set forth above are not considered as growth factors, these agents are the growth or differentiation agents. Thus, the culture medium itself recited in claim 54 has already

contained more than one growth or differentiation agents. However, the claim itself also recites that the gp130 activator is the only growth or differentiation agent, which is in conflict with the fact that the culture medium contains more than one growth or differentiation agents. Accordingly, the recitation of "the gp130 activator is the only growth or differentiation agent present in the culture medium encompasses a broad range or limitation (i.e. culture medium itself containing a lot of growth agents) together with a narrow range or limitation that falls within the broad range or limitation (in the same claim), which is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Accordingly, the rejection of claim 54 under 35 U.S.C. 112, second paragraph, as being indefinite is maintained.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 7, 8 and 54-60 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6562619 (Gearhart et al. issued on May 13, 2003, priority Mar 31, 1998, cited previously) in view of Zhang et al. (Nat Biotechnol. 2001, Dec, 1129-1133, as in IDS) as evidenced by Baumann et al. (Physiol. Rev. 2001. 81:871-927) and Billon et al. (J. Cell Sci. 2002. 115: 3657-3665, as in IDS).

Claims 1, 3, 5, 7, 8 and 54-60 are drawn to a method of generating O1⁺ and/or O4⁺ oligodendrocytes comprising growing neurosphere (NS) cells in a culture medium that promotes differentiation of NS cells into O1⁺ and/or O4⁺ oligodendrocytes, said culture medium comprising one or more gp130 activators selected from the group consisting of CNTF, oconstatin-M (OSM) or IL-6, IL6R/IL6 chimera and IL-11 and wherein said culture medium specifically enhances differentiation into O1+ and/or O4+

oligodendrocyte lineage, thereby causing the NS cells to differentiate along the oligodendrocyte lineage into O1+ and/or O4+ oligodendrocyte lineage. Dependent claims 54 and 60 are directed to one or more gp130 activator is the only growth or differentiation agent and dependent claims 56 and 57 are directed to the culture medium promotes myelinating activity and formation of large and highly branched O+ and/or O4+ oligodendrocytes exhibiting large myelin membranes.

On p. 11-12 of the response, Applicant argues that the starting material in the claimed method is neurospheres but Greahart does not teach neurospheres because Greahart fails to teach neurospheres derived from embryoid bodies. Applicant argues that embryoid bodies derived from embryonic stem cells are not the same as neurospheres as supported by Carpenter. On p. 13 of the response, Applicant argues that Gearhart fails to disclose a method using a culture medium that promotes preferential differentiation into oligodendrocytes as claimed because Gearhart only teaches generalized differentiation and not how to obtain preferential differentiation into oligodendrocytes. Applicant argues that the methods of Gearhart result in a mixture of cells, which are different from those in instant claims. Applicant argues that neurospheres are not necessarily present in the cells or methods of Gearhart. On p. 14 of the response, Applicant argues that the primary reference does not disclose expression of O1+ and O4+ markers on differentiated oligodendrocytes. Applicant's arguments have been fully considered but they are not persuasive.

In response, Applicant cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case, Gearhart (the '619 patent) teaches a method of differentiating oligodendrocytes comprising growing embryonic stem (pPS) cells including mouse and human embryonic stem cells in the presence of a gp130 activator including IL-6 and IL-11 as recited in instant claims (see col. 28, example 6; col. 30, claims 1-28, in particular). Gearhart teaches that embryonic stem (ES) cells cultured in a standard culture medium form embryoid bodies, the embryoid body cells were re-suspended and passaged through 1-3 passages (7 to 30 days), replated in insulin-transferin-selenium-fibronectin (ITSN) supplemented medium dissociated and replated into medium containing basic fibroblast growth factor (bFGF) (see col. 29, lines 29-40; col. 30, claim 9; col. 24-25, examples 1-2 and 6; col. 15, lines 16-col. 16, line 9, in particular). Gearhart teaches that upon removal of FGF, neurons, astrocytes, and oligodendrocytes are expected to form in situ, and that the culture medium for differentiation contains FGF, LIF and IL-6, IL-11, oncostatin-M (OSM) or LIF (i.e. a gp130 activator) (see col. 28, example 6; col. 30, claims 1-28, col. 14, line 27-col. 15, line 4; see p. 237, abstract; p. 237, 2nd col.-p. 238, 1st col., in particular). Thus, Gearhart does teach a method of generating oligodendrocytes from cells derived from cultured human ES cells and the human ES-derived cells have been through several passages of dissociation resuspension, replating and culturing from embryoid bodies.

Although Gearhart does not explicitly teach neurospheres derived from embryoid bodies, Zhang et al. teach that human embryonic stem (ES) cells cultured in a defined medium containing FGF-2 (bFGF) for a week differentiate into O4+, O1+ and GFAP+ neural precursor cells (see p. 1129-1130, in particular). Zhang further teaches that when continuing exposure to FGF-2, the above isolated human ES-derived neural precursor cells can form columnar rosette cells (i.e. embryoid bodies). In addition, Zhang teaches that when the above cells were expanding as free-floating cell aggregates in a suspension culture, these human ES-derived neurosphere can be maintained up to 8 passages and can be differentiated into neurons and glia in a similar pattern as early passages. Zhang further teaches that upon removal of FGF-2 (bFGF), the above cells can be differentiated into neurons, glia and oligodendrocytes (see p. 1129, in particular). Note that based on the teaching of Zhang, human derived-ES cells can form embryoid bodies and neurospheres in the culture of human ES cells in the presence of FGF-2 as evidenced by Billon et al. (see p. 3658, 2nd Col., 3rd paragraph-p. 3659, 1 st col., 2nd paragraph, in particular, *J. Cell Sci.* 2002;115: 3657-3665, as in IDS). Thus, the cells through 1-3 passages of re-dissociation, resuspension and repassages from embryoid bodies (i.e. originally derived from embryonic stem cells) taught by Gearhart would also give rise to neurospheres because the cells cultured in the method of Gearhart are re-suspended and passaged and cultured in the same manner as the cells in Zhang and as in instant specification (col. 24-25, examples 1-2 and 6, in particular). Thus, the cells derived from embryoid bodies as taught by Gearhart would have similar properties as neurospheres recited instant claim 1.

Although Gearhart does not explicitly teach expression O4⁺ and O1⁺ markers on differentiated oligodendrocytes as recited in instant claims 1, 7, 8, 57 and 60, Zhang et al. teach that human embryonic stem (ES) cells cultured in a defined medium containing FGF-2 (bFGF) for a week differentiate into O4+, O1+ and GFAP+ neural precursor cells (see p. 1129-1130, in particular) and the markers for differentiated oligodendrocytes include O4+ and O1+ as evidenced by Baumann et al. (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular, Physiol. Rev. 2001. 81:871-927, cited previously). It would have been obvious to a skilled artisan at the time the instant invention was made to use neurospheres or human ES-derived neurospheres in the method of Gearhart to generate O1+ and/or O4+ oligodendrocytes in the presence of a gp130 activator such as CNTF, OSM, LIF, IL-6 or IL-11. The skilled artisan would have been motivated to do so with an expectation of success because neurospheres can be derived from embryoid bodies from cultured human ES as taught by Zhang and the cells expanded and re-suspended from embryoid bodies that are originally derived from human ES cells in the presence of a gp130 activator such as CNTF, OSM, LIF, IL-6 or IL-11 can be differentiated into O1+ and/or O4+ oligodendrocytes as taught by Gearhart.

The instant method is obvious over the cited references because the instant method is to simply replace "the cells derived from embryoid bodies" with "neurospheres" in the method of Gearhart because cells expanded or derived embryoid bodies would have similar properties derived from neurospheres and cells derived embryoid bodies cultured in a free-floating suspension would give rise to neurospheres. Thus, the results from the claimed are expected.

On p. 14-17 of the response, Applicant argues that Zhang does not disclose or suggest steps for the differentiation of ES cells toward specific cell lineages such as myelinated oligodendrocytes. Applicant argues that the instant invention is an improvement over the method in Zhang. Applicant argues that Zhang does not provide motivation to modify the method of Gearhart to solely use neurospheres in the claimed method. Applicant's arguments have been fully considered but they are not persuasive.

Contrary to Applicant's arguments, Zhang does teach steps for differentiation of human ES cells toward specific cell lineages such as O4+, O1+ oligodendrocytes (see p. 1129-1130, in particular). In addition, the Zhang reference is to support the cells in the method of Gearhart are capable of differentiating into O4+, O1+ oligodendrocytes and is also to support that human derived-ES cells can form embryoid bodies and neurospheres in the culture of human ES cells in the presence of FGF-2 in the method of Gearhart as evidenced by Billon et al. (see p. 3658, 2nd Col., 3rd paragraph-p. 3659, 1st col., 2nd paragraph, in particular, J. Cell Sci. 2002.115: 3657-3665, as in IDS).

On p. 17-18 of the response, Applicant argues that the gp130 activator does not exert the same effect on embryoid bodies as it does not neurospheres. Applicant argues that embryoid bodies treated with IL6RIL6 resulted in no expression of oligodendrocyte lineage-specific gene expression whiles neurospheres treated with IL6RIL6 resulted in marked increase in expression and cites example 5 of the

specification (see p. 35-36) in support of the arguments. Applicant's arguments have been fully considered but they are not persuasive.

In response, Applicant's arguments regarding to no enhancement of specific gene expression in embryoid bodies when treated with a gp130 activator are irrelevant because the cells used in the method of Gearhart to differentiate into oligodendrocytes are not embryoid bodies. Instead, the cells used in the method of Gearhart are the cells derived from the embryoid body cells after culturing several passages of the cells dissociated from embryoid bodies. Although Gearhart does not explicitly use the term "neurospheres", embryoid bodies after dissociation, resuspension, replating and culturing several passages, the cells are called neurospheres and can be differentiated into neurons and glia in a similar pattern as early passages as supported by Zhang. Zhang teaches that columar rosette cells (i.e. embryoid bodies) cultured from human ES-derived neural precursor cells after expending as free-floating cell aggregates in a suspension culture are called human ES-derived neurospheres; and these human ES-derived neurosphere can be maintained up to 8 passages and can be differentiated into neurons and glia in a similar pattern as early passages.

On p. 18-19 of the response, Applicant argues that Gearhart relates to differentiation into a mixture of neuronal cells in general but does not teach the use of a culture medium in a method to specifically enhance differentiation to cause the NS cells to differentiate along the oligodendrocyte lineage into O1+ and/or O4+

oligodendrocytes. Applicant's arguments have been fully considered but they are not persuasive.

Contrary to Applicant's arguments, Gearhart does teach the culture medium for differentiation into oligodendrocytes wherein the medium contains FGF, LIF and IL-6 or IL-11 (see col. 28, example 6; col. 30, claims 1-28, col. 14, line 27-col. 15, line 4 in particular). Gearhart also teaches a method of differentiating oligodendrocytes comprising growing embryonic stem (pPS) cells including mouse and human embryonic stem cells in the presence of a gp130 activator including IL-6, IL-11, LIF, or oncostatin-M as recited in instant claims (see col. 28, example 6; col. 30, claims 1-28, in particular).
(i). In particular, Gearhart teaches that upon removal of FGF, neurons, astrocytes, and oligodendrocytes are expected to form in situ (col. 15, lines 16-col. 16, line 9; see col. 28, example 6; col. 30, claims 1-28, col. 14, line 27-col. 15, line 4 in particular). Note that the instant claims are not limited to generate a specific proportion of O1+/O4+ oligodendrocytes. As long as the method of Gearhart can generate oligodendrocytes that are O1 and/or O4 positive, the teaching of Gearhart meets the limitations recited in instant claims. In addition, although Gearhart does not explicitly teach that oligodendrocytes are O4+ and O1+, Baumann teaches that markers of differentiated oligodendrocytes including O4+ and O1+ (see p. 875, 2nd col, 2nd-3rd paragraphs, in particular) and Zhang teaches that human embryonic stem (ES) cells cultured in a defined medium containing FGF-2 (bFGF) for a week differentiate into O4+, O1+ and GFAP+ neural precursor cells (see p. 1129-1130, in particular). Thus, Gearhart does teach a culture medium for differentiation of oligodendrocytes.

On p. 18-19 of the response, Applicant argues that the combination of Gearheart and Zhang fails to disclose or suggest each and every element of the claims. Applicant argues that the references of Bauman and Billon do not resolve the deficiencies of Gearhart and Zhan because Billon relates to a study of timing of oligodendrocyte development from genetically engineered-selectable mouse ES cells and Billon does not teach the use of neurospheres. Applicant's arguments have been fully considered but they are not persuasive.

In response, Applicant cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case, Gearhart (the '619 patent) teaches a method of differentiating oligodendrocytes comprising growing embryonic stem (pPS) cells including mouse and human embryonic stem cells in the presence of a gp130 activator including IL-6 and IL-11 as recited in instant claims (see col. 28, example 6; col. 30, claims 1-28, in particular). Gearhart teaches that embryonic stem (ES) cells cultured in a standard culture medium form embryoid bodies (see col. 29, lines 29-40; col. 30, claim 9). Gearhart teaches that the embryoid body cells were re-suspended and passaged through 1-3 passages (7 to 30 days) (col. 24-25, examples 1-2 and 6, in particular) and replated in insulin-transferin-selenium-fibronectin (ITSN) supplemented medium dissociated and replated into medium containing basic fibroblast growth factor (bFGF) (col. 15, lines 16-col. 16, line 9, in particular). Gearhart teaches that upon removal of

FGF, neurons, astrocytes, and oligodendrocytes are expected to form *in situ*, and that the culture medium for differentiation contains FGF, LIF and IL-6, IL-11, oncostatin-M (OSM) or LIF (i.e. a gp130 activator) (see col. 28, example 6; col. 30, claims 1-28, col. 14, line 27-col. 15, line 4; see p. 237, abstract; p. 237, 2nd col.-p. 238, 1st col., in particular)

Although Gearhart does not explicitly teach neurospheres derived from embryoid bodies, Zhang et al. teach that human embryonic stem (ES) cells cultured in a defined medium containing FGF-2 (bFGF) for a week differentiate into O4+, O1+ and GFAP+ neural precursor cells (see p. 1129-1130, in particular). Zhang further teaches that when continuing exposure to FGF-2, the above isolated human ES-derived neural precursor cells can form columnar rosette cells (i.e. embryoid bodies). In addition, Zhang teaches that when the above cells were expanding as free-floating cell aggregates in a suspension culture, these human ES-derived neurosphere can be maintained up to 8 passages and can be differentiated into neurons and glia in a similar pattern as early passages. Zhang further teaches that upon removal of FGF-2 (bFGF), the above cells can be differentiated into neurons, glia and oligodendrocytes (see p. 1129, in particular). Note that based on the teaching of Zhang, human derived-ES cells can form embryoid bodies and neurospheres in the culture of human ES cells in the presence of FGF-2 as evidenced by Billon et al. (see p. 3658, 2nd Col., 3rd paragraph-p. 3659, 1 st col., 2nd paragraph, in particular, *J. Cell Sci.* 2002;115: 3657-3665, as in IDS). Thus, the cells through 1-3 passages of re-dissociation, resuspension and repassages from embryoid bodies (i.e. originally derived from embryonic stem cells) taught by Gearhart would also

give rise to neurospheres because the cells cultured in the method of Gearhart are re-suspended and passaged and cultured in the same manner as the cells in Zhang and as in instant specification (col. 24-25, examples 1-2 and 6, in particular). Thus, the cells derived from embryoid bodies as taught by Gearhart would have similar properties as neurospheres recited instant claim 1.

Although Gearhart does not explicitly teach expression O4⁺ and O1⁺ markers on differentiated oligodendrocytes as recited in instant claims 1, 7, 8, 57 and 60, Zhang et al. teach that human embryonic stem (ES) cells cultured in a defined medium containing FGF-2 (bFGF) for a week differentiate into O4+, O1+ and GFAP+ neural precursor cells (see p. 1129-1130, in particular) and the markers for differentiated oligodendrocytes include O4+ and O1+ as evidenced by Baumann et al. (see p. 875, 2nd col, 2nd -3rd paragraphs, in particular, Physiol. Rev. 2001. 81:871-927, cited previously). It would have been obvious to a skilled artisan at the time the instant invention was made to use neurospheres or human ES-derived neurospheres in the method of Gearhart to generate O1+ and/or O4+ oligodendrocytes in the presence of a gp130 activator such as CNTF, OSM, LIF, IL-6 or IL-11. The skilled artisan would have been motivated to do so with an expectation of success because neurospheres can be derived from embryoid bodies from cultured human ES as taught by Zhang and the cells expanded and re-suspended from embryoid bodies that are originally derived from human ES cells in the presence of a gp130 activator such as CNTF, OSM, LIF, IL-6 or IL-11 can be differentiated into O1+ and/or O4+ oligodendrocytes as taught by Gearhart.

The instant method is obvious over the cited references because the instant method is to simply replace "the cells derived from embryoid bodies" with "neurospheres" in the method of Gearhart because cells expanded or derived embryoid bodies would have similar properties derived from neurospheres and cells derived embryoid bodies cultured in a free-floating suspension would give rise to neurospheres. Thus, the results from the claimed are expected. Obviousness is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR International Co. V. Teleflex Inc.* 82 USPQ2d 1385 (2007). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Conclusion

6. NO CLAIM IS ALLOWED.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.

February 14, 2011

/Chang-Yu Wang/
Examiner, Art Unit 1649